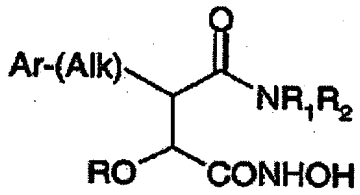
The listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1. (Original) A compound of formula (I), or an enantiomer or diastereoisomer thereof, or a salt, hydrate or solvate thereof:



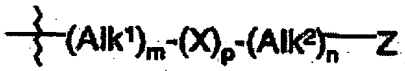
(I)

wherein Ar represents an optionally substituted aryl, heteroaryl, C_3-C_8 cycloalkyl or heterocycloakyl group;

R represents hydrogen or C_1-C_6 alkyl, or C_3-C_6 cycloalkyl;

Alk represents a divalent C_1-C_5 alkylene or C_2-C_5 alkenylene radical; and

R_1 and R_2 taken together with the nitrogen atom to which they are attached form a first heterocycloalkyl ring which is optionally fused to a second C_3-C_8 cycloalkyl or heterocycloalkyl ring, the said first and second rings being optionally substituted by at least one group of formula (II):



(II)

wherein m, p and n are independently 0 or 1;

Z represents, hydrogen, or an optionally substituted carbocyclic or heterocyclic ring of from 5

to 7 ring atoms which is optionally fused to another optionally substituted carbocyclic or heterocyclic ring of from 5 to 7 ring atoms;

Alk^1 and Alk^2 independently represent optionally substituted divalent C_1-C_3 alkylene radicals;

X represents -O-, -S-, -S(O)-, -$S(O_2)$-, -C(=O)-, -NH-, -NR_3-, -$S(O_2)$NH-, -$S(O_2)NR_3$-, -$NHS(O_2)$-, or -$NR_3S(O_2)$-, where R_3 is C_1-C_3 alkyl.

2. (Original) A compound as claimed in claim 1 wherein R is hydrogen.

3. (Original) A compound as claimed in claim 1 wherein R is methyl.

4. (Original) A compound as claimed in claim 1 wherein R is ethyl, n-propyl, isopropyl, n-, sec- or tert-butyl, cyclopropyl, or cyclopentyl.

5. (Currently Amended) A compound as claimed in Claim 1 ~~any of the preceding claims~~ wherein Ar is a 5- or 6- membered monocyclic aryl or heteroaryl ring, which is optionally substituted by at least one substituent selected from (C_1-C_3)alkyl, (C_1-C_3)alkoxy, hydroxy, hydroxy(C_1-C_3)alkyl, mercapto, mercapto(C_1-C_3)alkyl, (C_1-C_3)alkylthio, halo, trifluoromethyl, trifluoromethoxy, nitro, nitrile (-CN), -COOH, -$COOR^A$, -COR^A,-SO_2R^A, -$CONH_2$, -SO_2NH_2, -$CONHR^A$, -SO_2NHR^A, -$CONR^AR^B$, -$SO_2NR^AR^B$, -NH_2, -NHR^A, -NR^AR^B, -$OCONH_2$, -$OCONHR^A$, -$OCONR^AR^B$, -$NHCOR^A$, -$NHCOOR^A$, -NR^BCOOR^A, -$NHSO_20R^A$, -$NR^BSO_2OR^A$, -$NHCONH_2$, -NR^ACONH_2, -$NHCONHR^B$, -NR^ACONHR^B, $NHCONR^AR^B$, or -$NR^ACONR^AR^B$ wherein R^A and R^B are independently C_1-C_3 alkyl, phenyl or a 5- or 6-membered monocyclic aryl or heteroaryl ring.

6. (Original) A compound as claimed in claim 5 wherein an optional substituent is in the 4-position in the case of a 6-membered ring, or in the 2- and/or 3- position in the case of a 5-membered ring.

7. (Currently Amended) A compound as claimed in Claim 1 ~~any of the preceding claims~~ wherein Ar is optionally substituted phenyl, 2-, 3-, or 4-pyridyl, 2-, or 3-thienyl, or 2-, or 3-

furanyl.

8. (Currently Amended) A compound as claimed in Claim 1 ~~any of the preceding claims~~ wherein optional substituents in Ar are selected from methoxy, ethoxy, trifluoromethoxy, methyl, ethyl, trifluoromethyl, hydroxyl, mercapto, fluoro, chloro, and bromo.

9. (Original) A compound as claimed in claim 5 wherein Ar is 4-(C_1C_3alkoxy)phenyl.

10. (Currently Amended) A compound as claimed in claim 5 wherein Ar is 4-ethoxyphenyl.

11. (Currently Amended) A compound as claimed in Claim 1 ~~any of the preceding claims~~ wherein Alk is $-CH_2-$, $-CH_2CH_2-$, $-CH_2CH(CH_3)-$, $-CH_2CH_2CH_2-$, $-CH_2CH_2CH_2CH_2-$, $-CH=CH-$, $-CH_2CH=CH-$, $-CH_2CH=CHCH_2-$, or $-CH=CHCH=CH-$.

12. (Currently Amended) A compound as claimed in Claim 1 ~~any of the preceding claims~~ wherein $-NR_1R_2$ forms a pyrrolidinyl, morpholyl, or thiomorpholyl ring.

13. (Currently Amended) A compound as claimed in Claim 1 ~~any of claims 1 to 11~~ wherein $-NR_1R_2$ forms a piperidinyl, or piperazinyl ring.

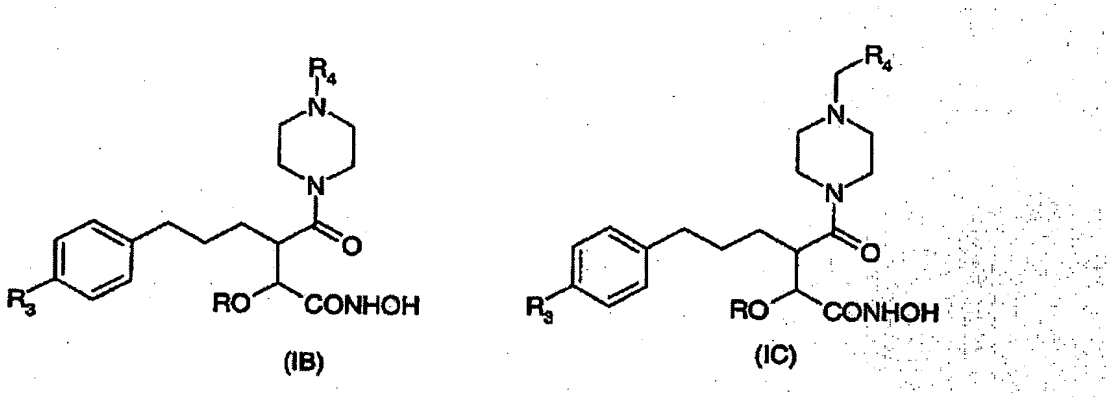
14. (Currently Amended) A compound as claimed in Claim 1 ~~any of the preceding claims~~ wherein in the group (II), when present, p is 0, Z is hydrogen and at least one of n and m is 1.

15. (Currently Amended) A compound as claimed in Claim 1 ~~any of claims 1 to 13~~ wherein in the group (II), when present, m, n and p are all 0 and Z is a carbocyclic or heterocyclic ring directly linked to a ring carbon or ring nitrogen of the $-NR_1R_2$ group.

16. (Currently Amended) A compound as claimed in Claim 1 ~~any of claims 1 to 13~~ wherein in the group (II), when present, p is 0, at least one of m and n is 1, and Z is a carbocyclic or heterocyclic ring linked to a ring carbon or ring nitrogen of the $-NR_1R_2$ group via a C_1-C_6 alkylene linker between Z and the $-NR_1R_2$ ring.

17. (Currently Amended) A compound as claimed in Claim 1 ~~any of claims 1 to 13~~ wherein in the group (II), when present, p is 1.

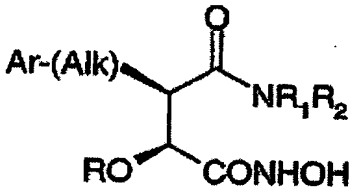
18. (Original) A compound as claimed in claim 1 of formula (1B) or (IC) or an enantiomer or diastereoisomer thereof, or a salt, hydrate or solvate thereof:



wherein R is hydrogen or methoxy, R_3 is trifluoromethyl, trifluoromethoxy C_1-C_3 alkoxy, hydroxy, or halo; R_4 is (i) -SO_2R_5 or -COR_5 wherein R_5 is C_1-C_6 alkyl or phenyl or monocyclic heteroaryl having 5 or 6 ring atoms, optionally substituted by (C_1-C_3)alkyl, (C_1-C_3)alkoxy, hydroxy, hydroxy(C_1-C_3)alkyl, mercapto, mercapto(C_1-C_3)alkyl, (C_1-C_3)alkylthio, halo, trifluoromethyl, trifluoromethoxy or (ii) phenyl or monocyclic heteroaryl having 5 or 6 ring atoms; optionally substituted by (C_1-C_3)alkyl, (C_1-C_3)alkoxy, hydroxy, hydroxy(C_1-C_3)alkyl, mercapto, mercapto(C_1-C_3)alkyl, (C_1-C_3)alkylthio, halo, trifluoromethyl, trifluoromethoxy.

19. (Original) A compound as claimed in claim 18 wherein a heteroaryl ring forming part of R_4 is pyridyl, pyrimidinyl, triazinyl, thienyl, or furanyl.

20. (Currently Amended) A compound as claimed in Claim 1 ~~any of the preceding claims~~ having the stereochemical configuration shown in formula (IA):



(IA)

21. (Currently Amended) A compound as claimed in claim 1, which is selected from the group consisting of:

6-(4-ethoxy-phenyl)-2S-hydroxy-3R-(pyrrolidine-1-carbonyl)-hexanoic acid hydroxyamide;

3R-(6, 7-dimethoxy-3,4-dihydro-1H-isoquinoline-2-carbonyl)-6-(4-ethoxyphenyl)-2S-hydroxy-hexanoic acid hydroxyamide;

6-(4-ethoxy-phenyl)-2S-hydroxy-3R-[4-(3-methoxy-phenyl)-piperazine-1-carbonyl]-hexanoic acid hydroxyamide;

6-(4-ethoxy-phenyl)-2S-hydroxy-3R-[4-(4-methoxy-phenyl)-piperazine-1-carbonyl]-hexanoic acid hydroxyamide;

6-(4-ethoxy-phenyl)-2S-hydroxy-3R-(4-pyridin-2-yl-piperazine-1-carbonyl)hexanoic acid hydroxyamide;

6-(4-ethoxy-phenyl)-2S-hydroxy-3R-(4-pyridin-4-yl-piperazine-1-carbonyl)-hexanoic acid hydroxyamide;

6-(4-ethoxy-phenyl)-2S-hydroxy-3R-(morpholine-4-carbonyl)-hexanoic acid hydroxyamide.

6-(4-ethoxy-phenyl)-2S-hydroxy-3R-(2RS-methyl-morpholine-4-carbonyl)-hexanoic acid hydroxyamide;

6-(4-ethoxy-phenyl)-2S-hydroxy-3R-(2,6-RS-dimethyl-morpholine-4-carbonyl)-hexanoic acid hydroxyamide;

6-(4-ethoxy-phenyl)-2S-hydroxy-3R-(thiomorpholine-4-carbonyl)-hexanoic acid hydroxyamide;

3R-(4-benzyl-piperidine-1-carbonyl)-6-(4-ethoxy-phenyl)-2S-hydroxy-hexanoic acid hydroxyamide;

3R-(4-benzo[1,3]dioxol-5-ylmethyl-piperazine-1-carbonyl)-6-(4-ethoxyphenyl)-2S-hydroxy-hexanoic acid hydroxyamide;

6-(4-ethoxy-phenyl)-2S-hydroxy-3R-(4-pyridin-4-ylmethyl-piperazine-1-carbonyl)-hexanoic acid hydroxyamide;

6-(4-ethoxy-phenyl)-2S-hydroxy-3R-(4-benzylpiperazine-1-carbonyl)-hexanoic acid hydroxyamide;

6-(4-ethoxy-phenyl)-2S-hydroxy-3R-(4-pyrimidin-2-yl-piperazine-1-carbonyl)-hexanoic acid hydroxyamide;

6-(4-ethoxy-phenyl)-2S-hydroxy-3R-[4-(4-trifluoromethyl-pyrimidin-2-yl)-piperazine-1-carbonyl]-hexanoic acid hydroxyamide;

6-(4-ethoxy-phenyl)-2S-hydroxy-3R-[4-(4-chloro-pyrimidin-2-yl)-piperazine-1-carbonyl]-hexanoic acid hydroxyamide;

3R-[4-(4,6-dimethoxy~[1,3,5]triazin-2-yl)-piperazine-1-carbonyl]-6-(4-ethoxyphenyl)-2S-hydroxy-hexanoic acid hydroxyamide;

6-(4-ethoxy-phenyl)-2S-hydroxy-3R-[4-(3-trifluoromethyl-phenyl)-piperazine-1-carbonyl]-

hexanoic acid hydroxyamide;

6-(4-ethoxy-phenyl)-2S-hydroxy-3R-[4-(2-fluoro-phenyl)-piperazine-1-carbonyl]-hexanoic acid hydroxyamide;

3R-[4-(acetyl-methyl-amino)-piperidine-1-carbonyl]-6-(4-ethoxy-phenyl)-2S-hydroxy-hexanoic acid hydroxyamide;

6-(4-ethoxy-phenyl)-2S-hydroxy-3R-[4-(methyl-propyl-amino)-piperidine-1carbonyl]-hexanoic acid hydroxyamide;

6-(4-ethoxy-phenyl)-2S-hydroxy-3R-(3S-benzyl-morpholine-4-carbonyl)-hexanoic acid hydroxyamide;

6-(4-ethoxy-phenyl)-2S-hydroxy-3R-(3S-isobutyl-morpholine-4-carbonyl)-hexanoic acid hydroxyamide;

6-(4-ethoxy-phenyl)-2S-hydroxy-3R-(3S-phenyl-morpholine-4-carbonyl)-hexanoic acid hydroxyamide;

3R-(4-benzyl-3RS-methyl-piperazine-1-carbonyl)-6-(4-ethoxy-phenyl)-2S hydroxy-hexanoic acid hydroxyamide;

3R-(3S,-4-dibenzyl-piperazine-1-carbonyl)-6-(4-ethoxy-phenyl)-2S-hydroxyhexanoic acid hydroxyamide;

3R-(4-benzyl-3RS-phenyl-piperazine-1-carbonyl)-6-(4-ethoxy-phenyl)-2S-hydroxy-hexanoic acid hydroxyamide;

4-(4-benzo[1, 3]dioxol-5-ylmethyl-piperazin-1-yl)-2S, N-dihydroxy-4-oxo-3R-(4-trifluoromethoxy-benzyl)-butyramide;

3R-benzyl-2S, N-dihydroxy-4-morpholin-4-yl-4-oxo-butyramide;

3R-(4-Benzyloxy-benzyl)-2S, N-dihydroxy-4-oxo-4-piperidin-1-yl-butyramide;

2S, N-dihydroxy-3R-(4-hydroxy-benzyl)-4-oxo-4-piperidin-1-yl-butyramide;

4-(4-benzo[1, 3]dioxol-5-ylmethyl-piperazin-1-yl)-3R-(4-benzyloxy-benzyl)2S, N-dihydroxy-4-oxo-butyramide;

6-(3, 5-bis-trifluoromethyl-phenyl)-2S-hydroxy-3R-(morpholine-4-carbonyl)hexanoic acid hydroxyamide;

3R-(4-benzyl-piperidine-1-carbonyl)-6-(3,5-bis-trifluoromethyl-phenyl)-2S-hydroxy-hexanoic acid hydroxyamide;

6-(3, 5-bis-trifluoromethyl-phenyl)-2S-hydroxy-3R-(4-pyridin-2-yl-piperazine-1-carbonyl)-hexanoic acid hydroxyamide;

6-(3, 5-bis-trifluoromethyl-phenyl)-3R-(6, 7-dimethoxy-3,4-dihydro-1 H-isoquinoline-2-carbonyl)-2S-hydroxy-hexanoic acid hydroxyamide;

6-(3, 5-bis-trifluoromethyl-phenyl)-2S-hydroxy-3R-(pyrrolidine-1-carbonyl)-hexanoic acid hydroxyamide

3R-(2S-benzyl-4-methyl-piperazine-1-carbonyl)-6-(4-ethoxy-phenyJ)-2Shydroxy-hexanoic acid hydroxyamide;

6-(4-ethoxy-phenyl)-2S-hydroxy-3R-[4-(4-trifluoromethoxy-benzenesulfonyl)piperazine-1-carbonyl]-hexanoic acid hydroxyamide;

6-(4-ethoxy-phenyl)-2S-hydroxy-3R-[4-(toluene-4-sulfonyl)-piperazine-1-carbonyl]-hexanoic acid hydroxyamide;

3R-[4-(5-bromo-thiophene-2-sulfonyl)-piperazine-1-carbonyl]-6-(4-ethoxyphenyl)-2S-hydroxy-hexanoic acid hydroxyamide;

3R-[4-(5-benzenesulfonyl-thiophene-2-sulfonyl)-piperazine-1-carbonyl]-6-(4-ethoxy-phenyl)-2S-hydroxy-hexanoic acid hydroxyamide;

3R-[4-(4-butoxy-benzenesulfonyl)-piperazine-1-carbonyl]-6-(4-ethoxy-phenyl)2S-hydroxy-hexanoic acid hydroxyamide;

6-(4-ethoxy-phenyl)-2S-hydroxy-3R-[4-(4-methoxy-2,3, 6-trimethylbenzenesulfonyl)-piperazine-1-carbonyl]-hexanoic acid hydroxyamide;

3R-[4-(3,4-dimethoxy-benzenesulfonyl)-piperazine-1-carbonyl]-6-(4-ethoxyphenyl)-2S-hydroxy-hexanoic acid hydroxyamide;

6-(4-methoxy-phenyl)-2S-hydroxy-3R-[4-(2-fluoro-phenyl)-piperazine-1carbonyl]-hexanoic acid hydroxyamide;

6-(4-methoxy-phenyl)-2S-hydroxy-3R-(4-pyridin-2-yl-piperazine-1-carbonyl)-hexanoic acid hydroxyamide;

6-(4-fluoro-phenyl)-3R-[4-(2-fluoro-phenyl)-piperazine-1-carbonyl]-2S-hydroxy-hexanoic acid hydroxyamide;

6-(4-fluoro-phenyl)-2S-hydroxy-3R-(4-pyridin-2-yl-piperazine-1-carbonyl)-hexanoic acid hydroxyamide;

3R-(4-benzyl-2S-methyl-piperazine-1-carbonyl)-6-(4-ethoxy-phenyl)-2S-hydroxy-hexanoic acid hydroxyamide;

3R-(4-benzyl-2S-methyl-piperazine-1-carbonyl)-6-(4-methoxy-phenyl)-2S-hydroxy-hexanoic

acid hydroxyamide~~,~~;

3R-(4-benzyl-2S-i-butyl-piperazine-1-carbonyl)-6-(4-methoxy-phenyl)-2S-hydroxy-hexanoic acid hydroxyamide~~,~~;

3R-(4-benzyl-2S-methyl-piperazine-1-carbonyl)-6-(4-fluoro-phenyl)-2S-hydroxy-hexanoic acid hydroxyamide~~,~~;

3R-(4-benzyl-2S-i-butyl-piperazine-1-carbonyl)-6-(4-fluoro-phenyl)-2S-hydroxy-hexanoic acid hydroxyamide~~,~~;

4-[5-(4-ethoxy-phenyl)-2R-(1S-hydroxy-hydroxycarbamoyl-methyl)-pentanoyl]-2S-methyl-piperazine-1-carboxylic acid tert-butyl ester~~,~~;

4-[5-(4-ethoxy-phenyl)-2R-(1S-hydroxy-hydroxycarbamoyl-methyl)-pentanoyl]-2S-i-butyl-piperazine-1-carboxylic acid tert-butyl ester~~,~~;

4-[5-(4-methoxy-phenyl)-2R-(1S-hydroxy-hydroxycarbamoyl-methyl)-pentanoyl]-2S-methyl-piperazine-1-carboxylic acid tert-butyl ester~~,~~;

4-[5-(4-methoxy-phenyl)-2R-(1S-hydroxy-hydroxycarbamoyl-methyl)-pentanoyl]-2S-i-butyl-piperazine-1-carboxylic acid tert-butyl ester~~,~~;

4-[5-(4-fluoro-phenyl)-2R-(1S-hydroxy-hydroxycarbamoyl-methyl)-pentanoyl]-2S-methyl-piperazine-1-carboxylic acid tert-butyl ester.

4-[5-(4-fluoro-phenyl)-2R-(1S-hydroxy-hydroxycarbamoyl-methyl)-pentanoyl]-2S-i-butyl-piperazine-1-carboxylic acid tert-butyl ester~~,~~; and

6-(4-ethoxy-phenyl)-2S-methoxy-3R-[4-(2-fluoro-phenyl)-piperazine-1carbonyl]-hexanoic acid hydroxyamide.

22. (Currently Amended) A pharmaceutical composition comprising a compound as claimed in Claim 1 ~~any of the preceding claims~~, together with a pharmaceutically acceptable carrier.

23. (Currently Amended) A compound as claimed in Claim 1 ~~any of claims 1 to 21~~ for use as a medicament.

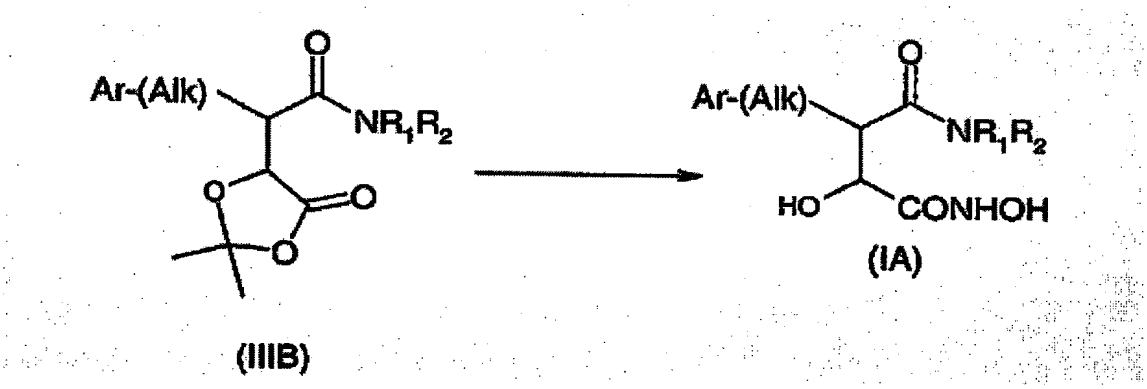
24. (Currently Amended) A method of treatment or prophylaxis of diseases or conditions responsive to inhibition of MMP-12 and/or MMP-9 in mammals, which method comprises administering to the mammal an effective amount of a compound as claimed in Claim 1. ~~any of claims 1 to 21~~

25. (Canceled)

26. (Currently Amended) A method as claimed in claim 24 ~~or a use as claimed in claim 25~~ wherein the disease or condition is bone resorption, tumour growth or invasion by secondary metastases; rheumatoid arthritis, septic arthritis, osteoarthritis, periodontitis, gingivitis, corneal ulceration, cardiac hypertrophy, acute respiratory distress syndrome, neuroinflammatory disorders, e.g. multiple sclerosis; restenosis; emphysemia; fibrotic ~~didease~~ disease e.g. fibrosis post radiotherapy, kerotid scarring, liver fibrosis and cystic fibrosis; chronic obstructive pulmonary disease; bronchitis; asthma; autoimmune disease; transplant rejection (e.g. graft versus host disease); cystic fibrosis; psoriasis; psoriatic arthritis; degenerative cartilage loss; inflammatory gastric conditions, e.g. Crohn's disease, inflammatory bowel disease, and ulcerative colitis; atopic dermatitis, epidermolysis bullosa; epidermic ulceration; a neuropathy or nephropathy e.g. interstitial nephritis, glomerulonephriris or renal failure; ocular inflammation; liver cirrhosis, Sjoegren's syndrome; or an inflammatory condition of the nervous system.

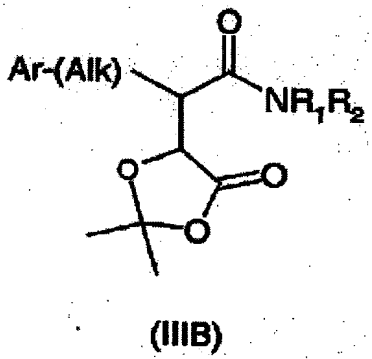
27. (Currently Amended) A method as claimed in claim 24 ~~or a use as claimed in claim 25~~ wherein the disease or condition is fibrotic disease, multiple sclerosis, emphysemia, bronchitis or asthma.

28. (Currently Amended) A method of preparing metalloproteinase inhibitors of formula (IA) according to Claim 1 ~~any of claims 1 to 21~~ wherein R is hydrogen, comprising the deprotection and/or transformation step of:



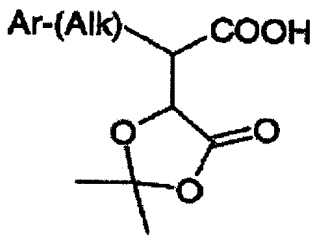
~~wherein Ar, Alk, R_1 and R_2 are as defined in Claim 1 any of claims 1 to 16~~.

29. (Currently Amended) A compound of formula IIIB



wherein Ar, Alk, R_1 and R_2 are as defined in Claim 1 ~~any of claims 1 to 19~~.

30. (Currently Amended) A process for the preparation of a compound as claimed in claim 29 comprising ~~comprising~~ the step of reacting a compound of formula (III)



(III)

with a cyclic amine HNR_1R_2; ~~wherein Ar, Alk, R_1 and R_2 are as defined in Claim 1 any of claims 1 to 19~~.

CONCLUSION

The claims were amended to place in proper U.S. format and eliminate multiple dependencies. No new matter was added by this amendment. Examination on the merits is respectfully requested.

Respectfully submitted,

Date: 2/14/06

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